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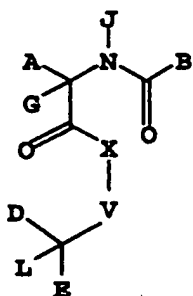
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(21) International Application Number: PCT/US98/17201 (22) International Filing Date: 19 August 1998 (19.08.98) (30) Priority Data: 60/056,135 19 August 1997 (19.08.97) US (71) Applicant (for all designated States except US): ELI LILLY AND COMPANY [US/US]; Lilly Corporate Center, Indianapolis, IN 46285 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): KAUFFMAN, Raymond, Francis [US/US]; 11420 Saint Andrews Lane, Carmel, IN 46032 (US). PALKOWITZ, Alan, David [US/US]; 10737 Kingsmill Drive, Carmel, IN 46032 (US). (74) Agents: STRODE, Janelle, D. et al.; Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: TREATMENT OF CONGESTIVE HEART FAILURE WITH GROWTH HORMONE SECRETAGOGUES		
(57) Abstract <p>The invention provides methods for the modulation of cardiac function by the administration of a growth hormone secretagogue, which results in an increase in the levels of endogenous growth hormone. Also provided are methods for the treatment of congestive heart failure by the administration of a growth hormone secretagogue. Further provided are methods for the treatment of congestive heart failure by the administration of a growth hormone secretagogue in combination with a growth hormone releasing hormone, or in combination with an antihypertensive agent, diuretic, or other suitable agents.</p>		

We Claim:

1. A method of modulating cardiac function which comprises administering to a patient in need thereof an effective amount of a growth hormone secretagogue.

2. A method according to Claim 1 wherein said growth hormone secretagogue comprises GRP-2.

3. A method according to Claim 1 wherein said growth hormone secretagogue comprises a compound of formula I

**I**

wherein:

A is C₁-C₆alkyl, aryl, C₁-C₆alkylaryl, C₁-C₆alkyl(O)C₁-C₆alkylaryl, C₁-C₆alkyl(S)C₁-C₆alkylaryl, indolyl, indolinyl, thienyl, (C₁-C₆alkyl)thienyl, benzothienyl, benzofuranyl, naphthanyl, cyclohexyl, (C₁-C₆alkyl)indolyl, (C₁-C₆alkyl)benzothienyl, (C₁-C₆alkyl)naphthanyl, (C₁-C₆alkyl)benzofuranyl, and (C₁-C₆alkyl)cyclohexyl;

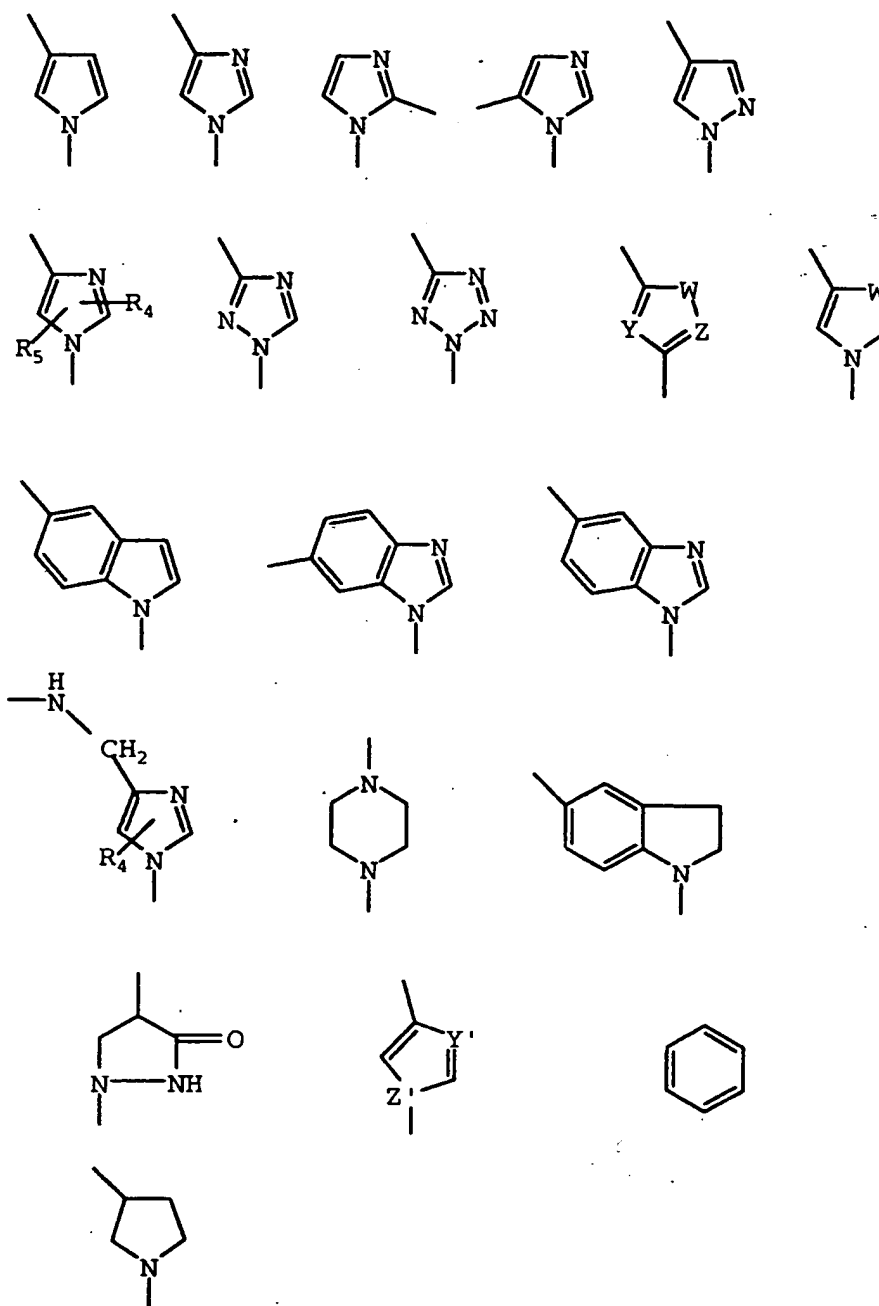
B is NH₂, NHR₁, C₁-C₆alkylNH₂, C₁-C₆alkylNHR₁, C₁-C₆alkylarylNH₂, C₁-C₆alkylarylNHR₁,

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- C₁-C₆alkylcyclohexylNH₂, C₁-C₆alkylcyclohexylNHR₁,
R₁-piperidin-3-yl(C₁-C₆alkyl),
R₁-piperidin-2-yl(C₁-C₆alkyl), R₁-piperidin-4-yl(C₁-C₆alkyl),
R₁-quinolin-2-yl(C₁-C₆alkyl),
5 R₁-(2,4-dihydroquinolin-2-yl(C₁-C₆alkyl),
R₁-isoquinolin-2-yl(C₁-C₆alkyl), and
R₁-(2,4-dihydroisoquinolin-2-yl(C₁-C₆alkyl);
R₁ is hydrogen, C₁-C₆alkyl, C₁-C₆alkyl(OH), or
C₁-C₆alkylidenyl(OH)R₂;
10 R₂ is C₁-C₆alkyl, C₁-C₆alkenyl,
C₁-C₆alkyl(O)C₁-C₆ alkyl, C(O)O-C₁-C₆ alkyl, aryl, or
C₁-C₆alkylaryl;
X is C₁-C₆alkylidenyl, O, S, NH, or N(C₁-C₆alkyl);
V is selected from the group consisting of

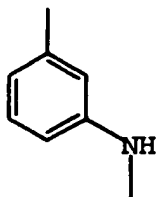
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and



- W is S, O, NH, or CH₂;
- 5 Y is N or CH;
- Z is N or CH;
- Y' is N or CH;
- Z' is N or CH;
- R₄ and R₅ are independently hydrogen, C₁-C₆alkyl,
- 10 aryl, C₁-C₆alkylaryl, C(O)O(C₁-C₆alkyl),
C(O)N(C₁-C₆alkyl)₂, or C₁-C₆alkylCOR₇;
- R₇ is hydrogen, C₁-C₆alkyl, pyrrolidinyl,
piperidinyl, homoproline, or proline;
- D is hydrogen, C₁-C₆alkyl,
- 15 C₁-C₆alkyl(O)(CO)C₁-C₆alkyl, C₁-C₆alkyl(O)(CO)N(C₁-C₆alkyl)₂,
C₁-C₆alkylaryl, C(O)R₆, C₁-C₆alkyl(O)R₆, C₁-C₆alkyl(OH), C₁-C₆
alkylC(O)R₆, C₁-C₆alkylR₆, aryl, (C₁-C₆alkyl)NHSO₂(C₁-C₆alkyl),
(C₁-C₆alkyl)NHSO₂(aryl);
- R₆ is H, C₁-C₆alkyl, aryl, naphthyl,
- 20 C₁-C₆alkylaryl, acetyl, NH₂, NH(C₁-C₆alkyl),
NH(C₁-C₆alkyl)O(C₁-C₆alkyl), NH(C₁-C₆alkyl)S(C₁-C₆alkyl),
NH(C₁-C₆alkylidenyl)OCH₃, NH(C₁-C₆alkyl)aryl,
NH(C₃-C₆ cycloalkyl), NH(C₁-C₆alkyl)C(O)(C₁-C₆alkyl),
NH(C₁-C₆alkyl)NH(C₁-C₆alkyl), NH(C₁-C₆alkyl)NH(C₁-C₆alkylaryl),
- 25 NHSO₂(C₁-C₆alkylaryl), NH(C₁-C₆alkyl)C(O)O(C₁-C₆alkyl),
NH(naphthyl), N(C₁-C₆alkyl)₂, N(C₁-C₆alkyl)(aryl),
N(C₁-C₆alkyl)(C₁-C₆alkylaryl), O(C₁-C₆alkyl), O(aryl),
O(C₁-C₆alkylaryl), piperidinyl,
piperidinyl-C(O)NH(C₁-C₆alkyl), piperidinyl-C(O)NH(C₁-
- 30 C₆alkylaryl), piperidinyl-C(O)N(C₁-C₆alkyl)₂,
piperidinyl-C(O)N(C₁-C₆alkyl)(aryl),
pyrrolidinyl, pyrrolidinyl C(O)NH(aryl),

- pyrrolidinyl C(O)NH(C₁-C₆alkyl),
pyrrolidinyl C(O)N(C₁-C₆alkyl)₂,
pyrrolidinyl C(O)NH(C₁-C₆alkylaryl),
pyrrolidinyl C(O)NH(C₁-C₆alkyl)(aryl),
5 pyrrolinyl, morpholino, hexamethyleneimino,
heptamethyleneimino, quinolinyl, 2,4-dihydroquinolinyl,
1,2,3,4-tetrahydroquinolinyl,
2,4-dihydroisoquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl,
indolinyl, an amino acid selected from the group consisting
10 of proline, homoproline, glycine, alanine, valine, leucine,
isoleucine, tyrosine, tryptophan, phenylalanine, serine,
threonine, asparagine, glutamic acid, aspartic acid,
lysine, arginine, glutamine, histidine, cysteine, and
methionine, or a nitrogen-containing heterocycle selected
15 from the group consisting of